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Is centralization of ovarian cancer care warranted? A cost-effectiveness analysis

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ABSTRACT

Objective. To evaluate the cost-effectiveness of tertiary referral care for ovarian cancer patients in the Netherlands.

Methods. We collected clinical and registry data on 1077 newly diagnosed ovarian cancer patients treated from 1996–2003 in a random sample of Dutch hospitals. Decision modelling was used to compare the cost-effectiveness of treatment in general hospitals, semi-specialized hospitals, and tertiary care centers. The actual direct medical costs of ovarian cancer treatment were evaluated. Long-term outcomes in terms of costs, quality-adjusted life-years (QALYs), and incremental costs per QALY gained were estimated. To assess uncertainty, multivariable sensitivity analyses and scenario analyses were performed.

Results. Treatment of ovarian cancer patients in semi-specialized hospitals costs on average €882 more than in general hospitals (95% confidence interval −720 to 2462) and yields 0.12 additional QALYs (95% CI 0.02 to 0.22), resulting in an incremental cost-effectiveness ratio (ICER) of €7135. Patients treated in tertiary care centers incurred again higher costs (€10,591, 95% CI 8757 to 12,480) and also higher QALYs (0.10, 95% CI 0 to 0.21), resulting in an ICER of €102,642 compared to semi-specialized hospitals. If the optimal debulking rate in tertiary care centers would increase to 70%, costs could drop below €30,000 per QALY.

Conclusion. Current treatment of ovarian cancer patients in semi-specialized hospital settings is a cost-effective strategy, while treatment in tertiary care centers becomes only cost-effective when better surgical results would be achieved.

Introduction

Ovarian cancer is the most lethal gynecologic malignancy. In the Netherlands, the incidence is about 1100 patients per year and virtually all 100 hospitals provide primary treatment for these patients. Several studies in other countries have shown improved outcome after treatment in specialized hospitals [1–5]. As in many countries, a heated discussion about centralizing care for ovarian cancer patients is going on in the Netherlands.

Recently, we have investigated the influence of hospital specialization on treatment results in the Netherlands [6]. We observed that patients treated in (semi-)specialized hospital settings significantly more often received adequate surgery and survival was better in these settings [6]. Nevertheless, even in (semi-)specialized settings surgical outcomes were inferior to results described in literature [7,8]. Only high-volume specialized gynecologists achieved outcomes that were comparable to the results in specialized settings in other countries. These findings support the notion that care in high-volume, specialized settings is warranted for patients with ovarian cancer.

Thus far, however, little is known about the balance between costs and effects of centralized care. Bristow et al. studied the cost-effectiveness of centralized care for patients with advanced-stage ovarian cancer and used a decision model to compare two hypothetical extremes: treatment in a non-specialized setting attaining 25% optimal debulking rates versus treatment in specialized centers with 75% optimal debulking rates and intra-peritoneal chemotherapy [9]. They reported that centralized care for patients with ovarian cancer would result in cost-effective healthcare [9]. However, in the Netherlands, optimal debulking rates in non-specialized settings are slightly higher. Furthermore, intra-peritoneal chemotherapy is not routine care, not even in tertiary care centers.

Accordingly, to advance the ongoing discussion and support considered policy decisions we assessed the clinical benefits and costs of Dutch ovarian cancer treatment in tertiary care centers, semi-specialized and general hospital settings using actual patient data. Furthermore, the incremental cost-effectiveness in scenarios with the present and with optimal adequate surgery rates was evaluated.

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Methods

Model overview

A decision model was developed to evaluate the cost-effectiveness of treatment in three different hospital settings [10]. The model was based on actual patient data regarding 1077 ovarian cancer patients newly diagnosed between 1996 and 2003 in a random sample of 18 Dutch hospitals. The cohort we used has been described elsewhere [6]. Hospitals were categorized according to specialization. Tertiary care centers are specialized (usually university) hospitals which employ gynecologic oncologists. Semi-specialized hospitals are large community (and usually teaching) hospitals with a semi-specialized gynecologist. Semi-specialized gynecologists are not formally trained in oncology but operate on the majority of the ovarian cancer patients in the hospitals they work in. Non-specialized hospitals are general (usually non-teaching) hospitals without (semi-) specialized oncologic care. Patient and treatment characteristics were collected from patient records and hospital information systems.

The model includes both a first-line treatment phase and a long-term Markov model phase. The first-line treatment phase is structured as a decision tree; patients could receive optimal, suboptimal or no surgery, followed by chemotherapy or no adjuvant treatment (Fig. 1). We distinguished 17 first-line treatment options based on prevalence and prognosis of different disease stages [11]; distribution of patients across first-line treatment options was based on the actual proportions observed in our study cohort (Table 1). The ultimate purpose of the decision tree was to estimate, for each of the three hospital settings, the proportion of the patient cohort in each of the three health states after the first-line treatment phase: being progression-free, having residual or relapsed disease, and death.

The long-term phase is structured as a Markov model with cycles of three months in duration. Patients may transition between the three health states during each cycle. Patients who have residual disease after the first-line treatment phase continue in a single 'residual or relapsed disease' health state until they die. Patients who were progression-free after the first-line treatment phase can remain the 'progression-free' health state, die, or progress to have relapsed disease. The Markov model estimates long-term survival duration and costs conditional on the patient's status after the first-line treatment phase. Hence, the differences between hospital settings only relate to the first-line treatment phase.

Measurement of resource use

We used data on health care resource use of all 155 ovarian cancer patients treated between 2000 and 2003 in six of the participating hospitals, two hospitals for each type of setting. Information on the number of operations during first-line treatment phase and the duration of the first operation were obtained from patient records. Data on hospital admission were derived from the National Medical Register (LMR) maintained by Prismant. The number of outpatient clinic visits was derived from hospital information systems. Data on the number of ultrasounds, chest X-rays, CT scans, laboratory tests and pathological examinations were provided by the hospital's financial administration. The number of gifts and type of chemotherapy administered were obtained from the patient records from the total study cohort.

Costs

Total surgical costs depended on the operation time and included personnel costs (gynecologists and surgeons) and operating room costs. Costs per hour in the operating room were assumed to be similar for the different hospital settings. The total costs of the first-line treatment phase per hospital setting were determined according to disease stage, number of operations and administration of chemotherapy. The costs of follow-up in the progression-free period and of monitoring and treatment in the period with relapsed disease were also determined per hospital setting. All cost estimates were updated to 2006 Euros on the basis of the Dutch inflation indices (http://statline.cbs.nl) and presented in Web Table 1 [12–14].

Health outcomes

The health outcomes of interest were median overall survival and quality-adjusted life-years. Progression-free survival was defined as the period of time between the end of the first-line treatment phase and the clinical recurrence of the disease. The probability of disease recurrence and the risk of dying from ovarian cancer were estimated by using the life-table method. Because the probability of disease recurrence decreases with time, we estimated the probability of disease recurrence for each treatment course through two time intervals: in the first 3 years and at 3–5 years after the first-line treatment phase. We did not distinguish further according to hospital setting, because we assumed that the progression-free survival would first and foremost depend on disease stage and first-line treatment result rather than on the hospital setting. The short- and long-term risk of dying from ovarian cancer was estimated in the first year and at 1–5 years after recurrent ovarian cancer separately for patients with early-stage disease and for patients with advanced disease.

Quality-adjusted life-years (QALYs) were calculated by multiplying the time a person remained in a certain health state by the utility associated with that particular health state and subsequent summing over all health states. Utility weights for the health states of progression-free (0.85) and residual or relapsed ovarian cancer (0.65) were derived from data published in the literature [15,16].

Analysis

For the comparison between hospital settings, we used equal distributions of patients over the various disease stages for all hospital settings. Expected quality-adjusted life-years and costs for ovarian cancer treatment according to hospital setting were calculated over the ten-year time horizon and presented as mean per patient. Costs and effects were discounted at 4% per year [12]. The analysis of cost-effectiveness followed standard decision rules using expected costs and QALYs [17]. If the expected costs of one hospital setting exceeded the other without the expected gain in health benefits, then this strategy was dominated and the other was deemed the more cost-effective. If both the expected costs and health benefits of one setting exceeded the other, then the incremental cost-effectiveness ratio (ICER) was calculated as the incremental cost per additional QALY generated by the more effective setting. Ovarian cancer treatment in a certain hospital setting was considered cost-effective when the incremental cost-effectiveness ratio was below €20,000 per QALY gained. Parameter uncertainty was addressed by means of probabilistic sensitivity analysis and was expressed as cost-effectivenesss acceptability curves (details on the website). In addition, we evaluated a scenario in which the percentage of adequately staged and optimally debulked patients in tertiary care settings was assumed to be 90% and 70%, respectively. These rates have been considered feasible in specialized settings [7,8].

Results

Cohort

The total cohort consisted of 1077 patients. We excluded 198 patients because they could not be classified according to one of the pre-defined first-line treatment options, leaving 879 patients for the cost-effectiveness analysis. The majority of the excluded patients had advanced disease and underwent surgery but declined or otherwise

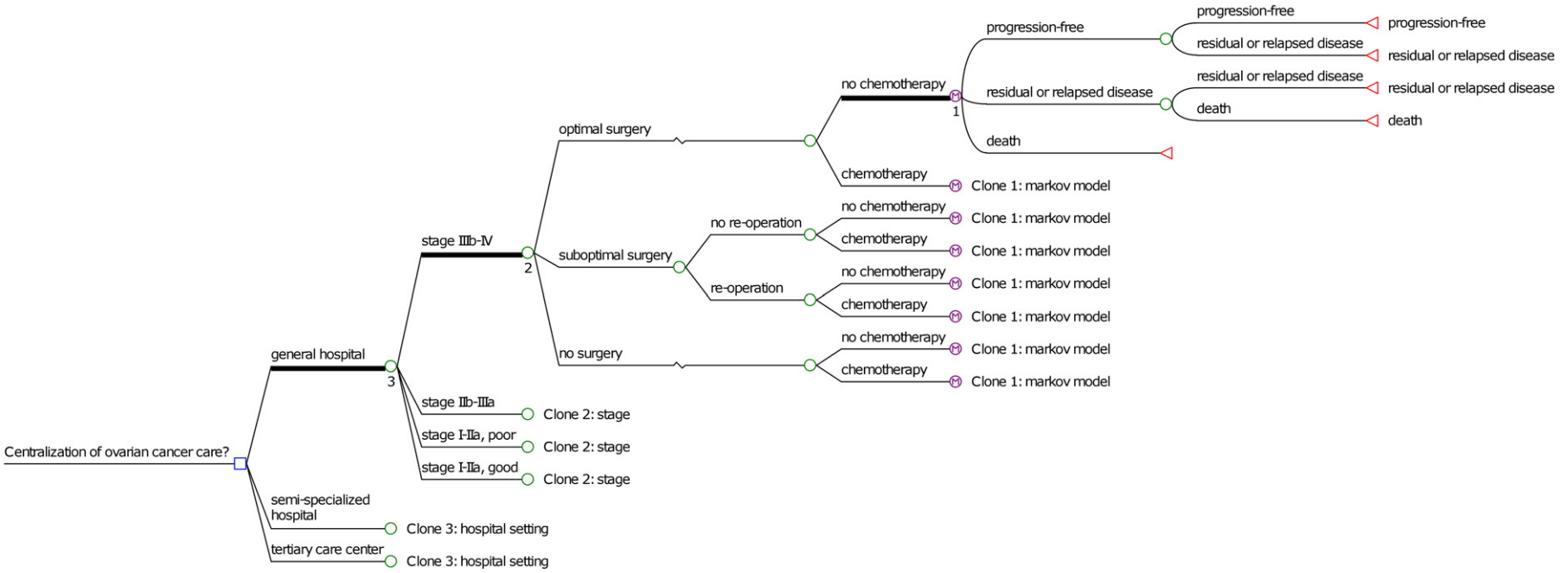

Fig. 1. General structure of the first-line treatment decision tree and long-term Markov model. The square node represents a decision node and circular nodes are chance nodes. The Markov model is shown by curved branches representing a single time cycle, with final outcomes representing by triangles, defining the state at the start of the subsequent cycle. The Markov model characterizes a patient's prognosis following the first-line treatment phase. Optimal surgery was defined as adequate staging (i.e. total abdominal hysterectomy, bilateral salpingo-oophorectomy, (partial) omentectomy, at least 1 lymph node removed and at least 1 peritoneal biopsy taken) in patients with stages I-IIa disease and as optimal cytoreduction (i.e. no residual tumor measuring greater than 1 cm in diameter) in patients with stages IIb-IV disease.

Table 1
Number and percentages of patients per first-line treatment option in different hospital settings

Course	Stage	Therapy	General hospitals		Semi-specialized hospitals		Tertiary care centers	
			$n=363$		$n=260$		$n=256$	
1	I–IIa, good*	Optimal surgery, no chemotherapy	6	(8%)	8	(18%)	10	(26%)
2	I–IIa, good	Non-optimal surgery, no chemotherapy	36	(50%)	11	(25%)	11	(28%)
3	I–IIa, good	Non-optimal surgery and chemotherapy	18	(25%)	8	(18%)	6	(15%)
4	I–IIa, good	Two operations, no chemotherapy	12	(17%)	17	(39%)	12	(31%)
5	I–IIa, poor**	Optimal surgery and chemotherapy	7	(28%)	2	(18%)	6	(46%)
6	I–IIa, poor	Non-optimal surgery, no chemotherapy	6	(24%)	3	(27%)	1	(8%)
7	I–IIa, poor	Non-optimal surgery and chemotherapy	12	(48%)	3	(27%)	6	(46%)
8	I–IIa, poor	Two operations and chemotherapy	0	(0%)	3	(27%)	0	(0%)
9	IIb–IIIa	Optimal surgery and chemotherapy	9	(22%)	12	(36%)	8	(26%)
10	IIb–IIIa	Non-optimal surgery and chemotherapy	25	(61%)	15	(45%)	15	(58%)
11	IIb–IIIa	Two operations and chemotherapy	7	(17%)	5	(15%)	5	(16%)
12	IIb–IIIa	No therapy	0	(0%)	1	(3%)	0	(0%)
13	IIIb–IV	Optimal debulking and chemotherapy	49	(22%)	51	(30%)	62	(36%)
14	IIIb–IV	Non-optimal debulking and chemotherapy	78	(35%)	53	(31%)	37	(21%)
15	IIIb–IV	Two debulking operations and chemotherapy	56	(25%)	42	(24%)	56	(32%)
16	IIIb–IV	No therapy	29	(13%)	18	(10%)	8	(5%)
17	IIIb–IV	Chemotherapy only	13	(6%)	8	(5%)	10	(6%)

* I–IIa good are patients with FIGO I or IIa with a low risk of recurrence (i.e. grade I or II, non-clear cell carcinoma) in whom chemotherapy was not indicated.
** I–IIa poor are patients with FIGO I or IIa with a high risk of recurrence (i.e. grade III or clear cell carcinoma) in whom chemotherapy was indicated [11].

did not get adjuvant chemotherapy. The mean age of our study population was 63 years; women in tertiary care centers tended to be somewhat younger. There were no significant differences between ovarian cancer patients with or without cost data with respect to surgical outcome, age and disease stage.

Treatment and effectiveness

Patients with early-stage disease (stages I–IIa) were more often adequately staged in more specialized hospitals (from general hospitals to tertiary care centers: 22%, 47% and 46% [$P=0.002$]). Patients with stage III disease were slightly more often optimally debulked in more specialized hospitals (from general hospitals to tertiary care centers: 37%, 41% and 46% [$P=0.3$]), but were also more frequently operated twice in these hospitals. Furthermore, general hospitals slightly more often refrained from therapy in patients with advanced disease. The proportion of patients in each of the 17 first-line treatment options differed between the hospital settings (Table 1). The differences in first-line treatment phase between the hospital settings resulted in better survival in more specialized hospitals (from general hospitals to tertiary care centers: predicted median survival was 3.6, 3.8 and 4.1 years).

Costs

A detailed overview of the most relevant cost estimates in the first-line treatment phase is presented in Web Table 2. The major cost component of first-line treatment was chemotherapy costs (from general hospitals to tertiary care centers: 44%, 41% and 38%). Operation costs accounted for approximately 9% of first-line treatment costs (from general hospitals to tertiary care centers: 11%, 10% and 9%). Total mean costs for each three months spent in the progression-free period showed no marked differences between the hospital settings (Table 2). Total mean costs in the residual or relapsed disease period were highest for patients treated in tertiary care centers. This was mainly due to the longer length of hospital stay during the period with residual or relapsed disease and the higher unit costs of inpatient hospital days and outpatient clinic visits in tertiary care centers.

Cost-effectiveness analysis

Expected costs, life-years and QALYs for ovarian cancer treatment according to hospital setting are presented in Table 3. The expected costs of ovarian cancer treatment were estimated to be €34,274 in general hospitals, €35,156 in semi-specialized hospitals and €45,748 in tertiary care centers. Ovarian cancer treatment in semi-specialized hospitals was estimated to produce 0.12 more QALYs compared to general hospitals. The incremental cost per QALY was estimated to be €7135. Ovarian cancer treatment in specialized hospitals was estimated to produce an additional 0.10 QALYs compared to semi-specialized hospitals. The incremental cost-effectiveness ratio of ovarian cancer treatment in tertiary care centers was estimated to be €102,642. Clearly, ovarian cancer treatment in semi-specialized hospitals had the lowest cost-effectiveness ratio (Fig. 2A). Results of the probabilistic sensitivity analysis are depicted in cost-effectiveness acceptability curves in Fig. 2B. The probability that ovarian cancer treatment in tertiary care centers is cost-effective is zero at a societal willingness-to-pay threshold of €20,000 per QALY. If a threshold of €100,000 per QALY gained would be considered acceptable, the probability that ovarian cancer treatment in tertiary care centers is

Table 2
Mean costs for each 3 months (ie, one Markov cycle) a patient spent in the progression-free, and residual or relapsed disease health state in different hospitals settings

	Mean costs per progression-free interval in the first 3 years*			Mean costs per period of residual or relapsed disease		
	General hospitals	Semi-specialized hospitals	Tertiary care centers	General hospitals	Semi-specialized hospitals	Tertiary care centers
Inpatient days	€3	€16	€23	€247	€571	€1218
Outpatient clinic visits	€71	€71	€127	€388	€388	€696
Laboratory tests	€147	€140	€122	€503	€466	€614
Chemotherapy	–	–	–	€1321	€1111	€910
Total costs	€221	€227	€272	€2459	€2536	€3438

* In the Netherlands, patients are monitored every 3 months in the first 3 years of the progression-free period, every 6 months after 3 years, and annually after 5 years [18]. Therefore, the progression-free costs estimates used in the model for the three to five years period were half, and beyond 5 years a quarter of the progression-free costs in the first 3 years.

Table 3
The expected mean costs and quality-adjusted life-years per patient in different hospital settings based on a 10-year time horizon

Setting	Effectiveness, QALYs	Incremental effectiveness*, QALYs (95%CI)		Costs, €	Incremental costs*, € (95%CI)		Incremental cost-effectiveness ratio*, €/QALY
Undiscounted							
General hospitals	3.53	–		36,111	–		–
Semi-specialized hospitals	3.67	0.14	(0.03 to 0.25)	37,054	943	(−707 to 2591)	6630
Tertiary care centers	3.79	0.12	(0.01 to 0.24)	48,403	11,350	(9489 to 13,239)	94,138
Optimal debulking in tertiary care centers	4.02	0.35	(0.23 to 0.47)	45,950	8896	(7172 to 10,695)	25,777
Discounted							
General hospitals	3.05	–		34,274	–		–
Semi-specialized hospitals	3.18	0.12	(0.02 to 0.22)	35,156	882	(−720 to 2462)	7135
Tertiary care centers	3.28	0.10	(0 to 0.21)	45,748	10591	(8757 to 12,480)	102,642
Optimal debulking in tertiary care centers	3.47	0.29	(0.19 to 0.40)	43,332	8176	(6379 to 10,026)	28,097

* Incremental effectiveness and incremental costs were determined by comparing general hospitals to semi-specialized hospitals and semi-specialized hospitals to tertiary care centers. The incremental cost-effectiveness ratio was calculated by dividing the incremental costs by the incremental effectiveness. Confidence intervals were derived from the Monte Carlo simulation (details on website).

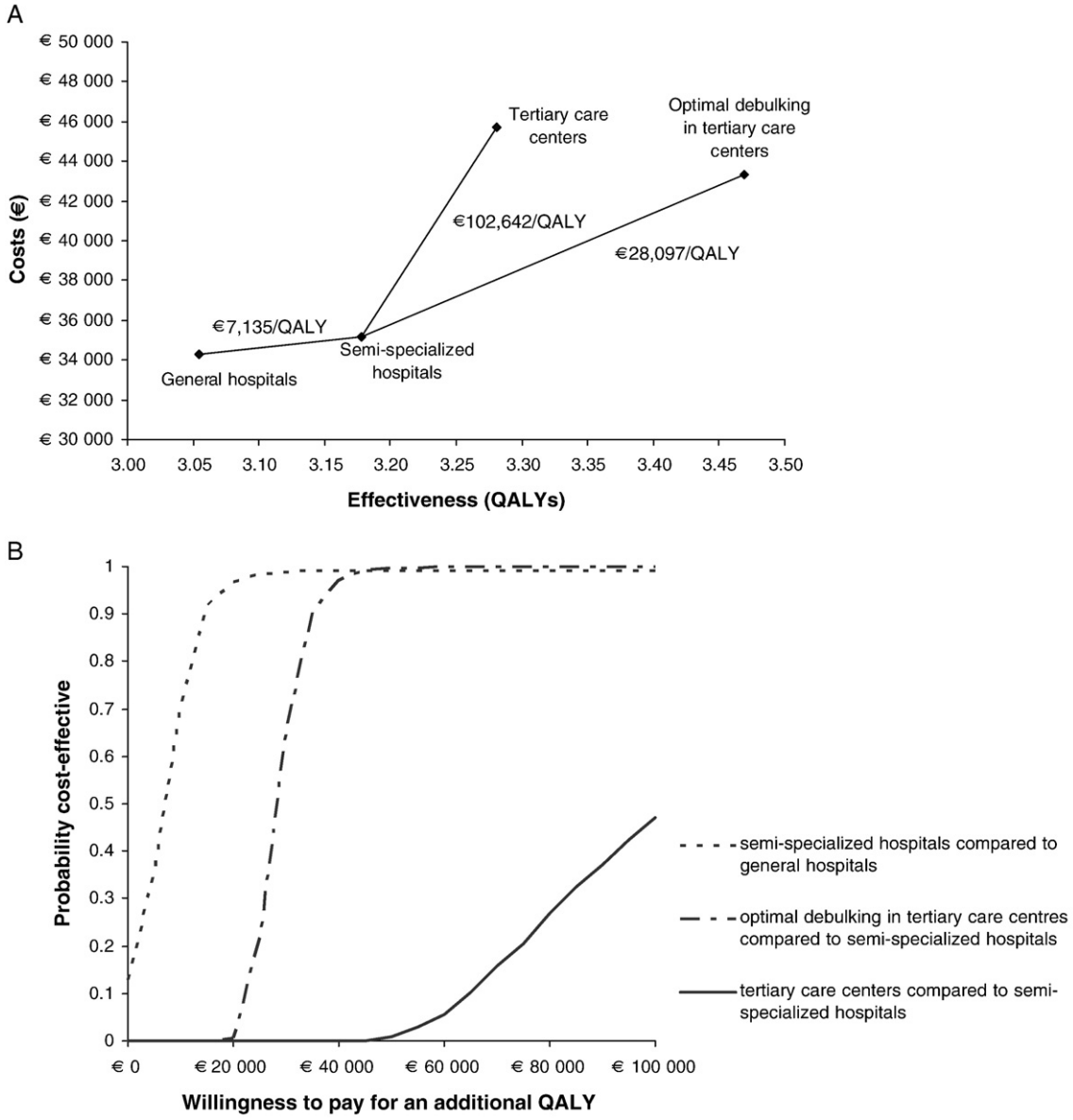

Fig. 2. (A) Average costs and effectiveness and incremental cost-effectiveness ratios for the different hospital settings. The incremental cost-effectiveness ratio is given by the slope of the line joining each successive hospital setting. (B) Cost-effectiveness acceptability curve. The *x*-axis shows a range of values that society may be willing to pay for an additional QALY, and the curve's elevation (on the *y*-axis) denotes the probability that ovarian cancer treatment for a certain hospital setting has a incremental cost-effectiveness ratio that is more favourable than the corresponding willingness-to-pay.

cost-effective would be 47%. Semi-specialized hospitals can be considered the preferred healthcare setting for ovarian cancer care, 96% of the estimates (as estimated with bootstrap replicates of the cohort) would fall below the threshold of €20,000 per QALY.

We conducted a scenario analysis to assess how the incremental (cost-) effectiveness ratio would change if the surgical results would be improved in tertiary care centers. If the percentages of adequately staged and optimally debulked patients in tertiary care settings would increase to 90% and 70%, respectively, ovarian cancer treatment in tertiary care centers was estimated to produce 0.29 QALYs more compared to semi-specialized hospitals. The incremental cost per QALY of ovarian cancer treatment in tertiary care centers was estimated to be approximately €28,000 (Table 3).

Discussion

The present study shows that treatment of ovarian cancer patients according to current practice patterns was most cost-effectively performed in semi-specialized hospital settings. Treatment in general hospitals resulted in worse health outcomes at virtually similar costs, whereas treatment in specialized hospital settings resulted in an additional survival benefit at much higher costs. However, if the optimal debulking rate in specialized hospitals would increase to 70%, ovarian cancer treatment in these hospitals also would become a cost-effective strategy.

These data signify that there is no place for treatment of ovarian cancer patients in general hospitals. Furthermore, the present results seem to argue against systematic referral of ovarian cancer patients to tertiary care centers. However, this analysis is based on data of patients treated between 1996 and 2003. In a previous study on this cohort we indicated that the results of semi-specialized and tertiary care settings were better than the results in general hospitals, but still lagged behind the outcomes described in literature [6–8]. The percentage of adequately staged patients should increase to 90% and the percentage of patients optimally debulked can be improved to at least 70% according to the literature [7,8]. Only gynecologic oncologists performing a high volume of ovarian cancer operations achieved these results. In the present study we showed that treatment of patients in such a high volume/centralized setting is a cost-effective strategy.

Our results roughly corroborate those by Bristow et al. [9]. They reported that centralized care of patients with advanced-stage ovarian cancer was cost-effective based on hypothetical debulking scenarios. The model used in the present study was more elaborate; we additionally took into account patients with early-stage disease, semi-specialized settings, and costs of follow-up and second-line treatment. Furthermore, almost all of our cost and effectiveness estimates were based on actual patient data, whereas Bristow et al. obtained clinical data and most of the cost estimates from the literature. The optimal debulking rates in our study population were higher in the nonspecialized settings and lower in the specialized settings than the hypothetical debulking rates of Bristow et al.[9].

We feel our study accurately represents current disparities between hospital settings. The study by Bristow et al. [9] provides support for the notion that surgical success is an important determinant of overall survival benefit and subsequently cost-effectiveness. Indeed, our scenario analyses evaluating a 70% optimal debulking rate in specialized hospitals indicated that referral to specialized hospitals would be a cost-effective strategy. The study of Bristow et al. [9] taken together with our own results provides strong support for the concept of a concentration of expertise to improve survival and cost-effectiveness.

Costs in specialized settings could be further reduced by introducing laparoscopic staging of patients with early-stage disease thereby reducing the number of inpatient days [19,20]. Furthermore, inpatient days during the relapsed disease period could be diminished by a professional, specialized and experienced homecare team taking care of patients in their own house thereby postponing admission until hospital care is really necessary. Another way to reduce costs could be to set up specialized clinics focused on tertiary referral care yet without the 'academic' components such as education and research. Referral of all pelvic masses would create logistical problems. Instead, pelvic masses with a small chance of being malignant can be distinguished from malignant tumors by using the Risk of Malignancy Index (RMI) [21]. Only patients with a RMI above the cutoff-level should be referred or operated in the hospital of diagnosis by a consulting specialized gynecologist.

Our analysis has certain limitations. Firstly, data were retrospectively gathered, and we could only count the items that were registered in patient records, hospital databases and national registers. However, information on the major cost components (surgery, inpatient days and chemotherapy) was documented accurately. Furthermore, we have no reason to believe that there are substantial differences between hospital settings in the registration of resource use, and therefore cost differences may assumed to be accurate. Secondly, we may have underestimated the effect of hospital specialization on treatment outcomes because patients in general hospitals were operated on by specialized gynecologists in one-fifth of the cases. Excluding these patients resulted in a more pronounced effect of specialization of hospital on survival [6]. We did not exclude these patients in the present study because we investigated the cost-effectiveness of the present system and surgery by a consulting specialized gynecologist is part of this system. Finally, we limited our analyses of costs to the direct medical costs. However, we do not think this will lead to a substantial underestimation of the total costs. The largest indirect costs would be the lost wages. However, the mean age of our population was 63 years and only a small proportion of the Dutch women in this age group has a paid job [22].

In conclusion, treatment of ovarian cancer patients in semi-specialized hospital settings is the most cost-effective strategy at the moment. If surgical care would be further optimized, referral to high-volume tertiary care settings also becomes cost-effective. Overall, a concentration of ovarian cancer expertise and care, and better training of specialized gynecologists seems warranted, while operating on this category of patients in general hospitals should no longer be considered acceptable practice.

Conflict of interest statement
None declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ygyno.2008.12.008.

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